CONDITION OF ENDOCRINE CELLS IN GASTRIC MUCOSA AFTER PENTAGASTRIN STIMULATION (AN EXPERIMENTAL STUDY)

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Key-word: gastric mucosa — endocrine cells — gastrin stimulation — hyperplasia — ulcer

Recently, endocrine cells (EC) of APUD-system from the upper parts of the digestive tract, and especially gastrin-producing cells (GC) are considered to play an essential role in the mechanisms of advanced hydrochloric acid hypersecretion in preulcerous conditions and duodenal ulcer (1—3, 5, 6). However, the data concerning EC specific action, the correlation interrelationships between them and the other specialized gastric cells, between the level of hormones produced and gastric juice acidity (1, 3, 14), etc. are still rather scanty and contradictory.

It is known that EC hormonal responcse in the stomach realizes mainly by the influence of adequate stimulators from its lumen (8). However, it is proved that exocytosis can be induced by hematogenic gastrin stimulation, too (15).

Proceeding from that we set us the task of investigating by means of light and electron microscope in experimental conditions of the condition of EC and mural cells in the gastric mucosa under hematogenic gastrin stimulation.

Material and methods

The experiment covered 30 white non-thoroughbred rats with 200 g mean b. w. 20 of them were daily s. c. injected 300 μg/kg b. w. pentagastrin solutions (according Tahara et al.). On the 2nd and 24th hour, as well as on the 2nd, 5th and 10th day 4 animals each were killed together with corresponding controls (a total of 10 controls). Material was taken from the glandular part of the stomach. It was fixed in 10 per cent neutral formalin and then the following stains were done on paraffin sections: HE, reaction with phospho-tungsten hematoxylin for selective ascertaining of mural cells, PAS reaction under α-amylase control, reaction with colloidal iron and alcyane blue, pH 1.5 for differentiation of gastric mucus components. Reactions of Grimelius and Sevier—Munger were used to detect argyrophilic EC and of Masson—Hamperl — argentafine ones. EC were counted at the average for visual field (plane of 0.045 mm^2) but mural cells were counted in a plane unit (0.022 mm^2 of the visual field) at magnification of the objective of 40.0 x. Data processing was carried out by the method of variation analysis. Small pieces of gastric mucosa were fixed in 2.5 per cent glutaraldehyde, postfixed in 1 per cent osmium tetraoxide and embedded in durcupan for electron microscopy. Ultrathin sections were contrasted with uranyl acetate and lead citrate and then examined under the electron microscope JEM 7A.

Results and discussion

We observed light microscopically in the gastric mucosa first of all argyrophilic EC ascertained by the reactions mentioned above. The number of these cells increased rapidly and statistically significantly in gastrin-stimulated animals already at the 2nd hour after application. Their number remained almost the same up to the 10th day (table 1). We failed to observe argentafine cells in this part of the gastric mucosa in the control animals. Single cells containing numerous granules occurred on the 5th day in experimental animals.

Table 1

Groups	Argyrophilic cells	Mural cells
Controls	9.9±0.6	39.5±5.3
2nd hr	20.5±0.9	34.0±3.2
	p<0.001	p<0.10
24th hr	15.6±2.5	87.0±2.9
	p<0.001	p<0.001
2nd day	19.0±2.0	79.0±2.9
	p<0.001	p<0.001
5th day	20.8±1.3	78.5±0.3
	p<0.001	p<0.001
10th day	20.2±2.3	65.0±4.7
	p<0.01	p<0.001

Electron-microscopically, there was an argyrophilic cell hyperplasia mainly on the account of enterochromaffin-like cells (ECL). In comparison with controls, they were seen very often and 2 hours after gastrin application they showed progressing up to the 10th day manifestations of massive degranulation — granules wrinkled, submembrane space dilatated strongly resulting in the formation of transparent, large, here and there fusing vacuoles with excentrically located rests of the material (fig. 1). More seldomly, D-cell could be seen. They contained many secretory granules, some of which were mature, electron-dense, other ones maturing, as well as single disaggregating ones. In this case the process described in ECL cells of degranulation more often was replaced by gradual loss of granular density with disappearing of membranes up to complete material disintegration in the cytoplasm or excentric rests of this material when «membrane skeleton» was restored (fig. 2). Basally, in both cell types an exocytosis was often established. It was observed on the lateral cell surface with D-cells, too (fig. 2).

A-like (or X) cells with mature granules without disintegration manifestations could also be found out (fig. 3). Single enterochromaffin cells were detected rather rarely, especially in experimental animals only (fig. 4). Similarly to A-like cells, they contained mainly mature granules.

We established an expressed parietalization corresponding to the rising EC number (table 1). The quantity of mural cells increased on the 24th hour almost twofold and remained high up to the 10th day (which was statistically reliable). Electron-microscopically, mural cells had features of massive functional activity — hyperproduction of tubuvesicles, numerous and large intracellular channels, dilatated outlet channels, a lot of mitochondria, etc.

On the 2nd hour we observed an oedema in the submucous membrane of the gastric mucosa, vascular congestion and plasmorrhagia. These alterations persisted if to a conciderably lower extent, up to the 10th day, too. In the first hours, and especially on the 2nd day after gastrin application mucus production in the mucosa enhanced mainly on the account of mucous cells from glandular cervices without any qualitative changes of mucus components. However, gradually on

the 5th and especially on the 10th day, surface and foveal mucus reduced accompanied with diminution of the content of sulfatized glucose-aminoglycans.

Our results obtained show that hematogenic gastrin application induces a considerable and permanent hyperplasia and functional activity mainly of ECL

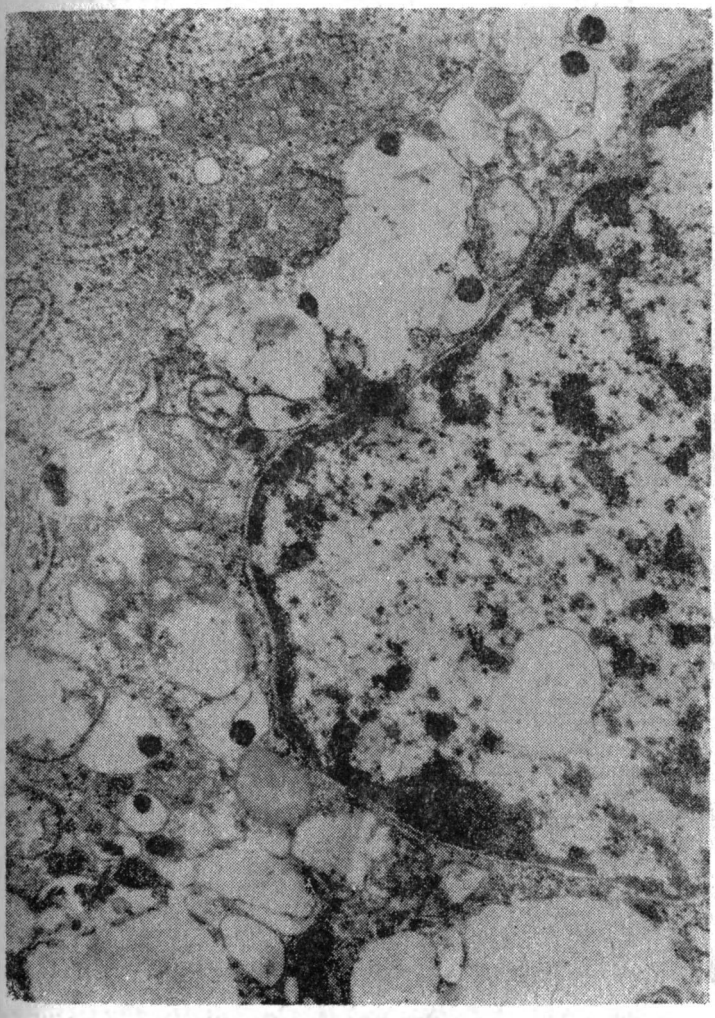

Fig. 1. ECL-cell with massive degranulation. Mag.x11000

cells in the glandular part of the stomach of experimental animals, as well as of D-cells to a lower extent. Single EC appear, too. A hyperplasia and hyperfunction of mural cells sets in correspondingly to ECL cell hyperplasia. It is proved in rats and mice that ECL cells produce histamine (9). Therefore, these cells are a link in the gastrin mechanism of mural cell stimulation in the processes of hydrochloric acid secretion although intimate mechanisms of gastrin and histamine interactions are not specified yet (4, 12, 15).

On the other hand, experimental data obtained confirm and explain the role and importance of the hyperplasia of gastrin-producing (G) cells in the antrum in the genesis of the hyperacidic state and duodenal ulcer in man which is already described by many investigators (1, 2, 6, 11, 16).

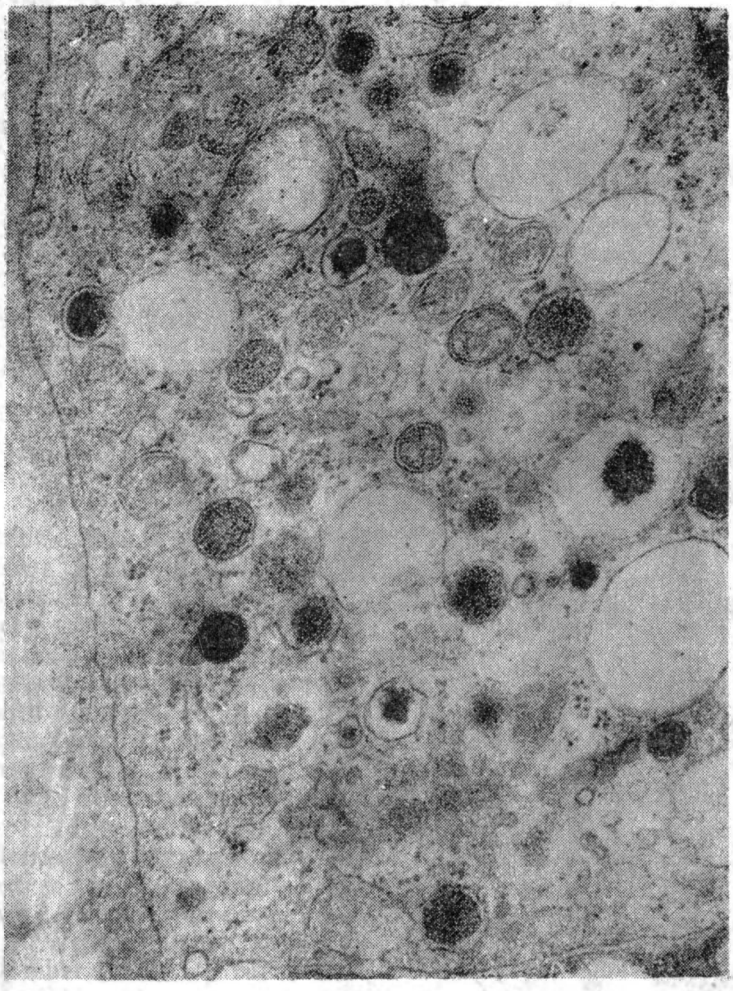

Fig. 2. D-cell with mature, maturing and disaggregating granules. Exocytosis on basal and lateral cell surface. Magn.x20 000

The weaker D-cell functional activity observed by us can be related with the inhibiting action of somatostatin produced by themselves (10) on the increased hydrochloric acid secretion caused by gastrin. Single enterochromaffin cells appear in the glandular part of the stomach as an expression probably of adaptation-compensatory mechanisms in conditions of enhanced functional activity of mural cells (6).

Gastric mucosa answers the gastrin-stimulated hydrochloric acid secretion by an increased mucus formation — by a defence-adaptation reaction which gradually decreases under the longlasting gastrin treatment (on the 5^{th}—10^{th} day) thus reducing the resistance of the mucosa and creating preconditions for secondary lesion of the gastric mucosa.

Fig. 3. A-like cell with mature granules. Magn.x 11000

Therefore, our results reveal the complex interrelations between endocrine, mainly G cells and ECL ones, on the one hand, and mural cells of the gastric mucosa, on the other hand, as well as the significance of the hormones produced by them in the morphogenesis of hyperacidic conditions and duodenal ulcer.

Fig. 4. Appearance of EC-cells with mature granules. Magn.x5000

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СОСТОЯНИЕ ЭНДОКРИННЫХ КЛЕТОК В СЛИЗИСТОЙ ОБОЛОЧКЕ ЖЕЛУДКА ПРИ СТИМУЛЯЦИИ ПЕНТАГАСТРИНОМ (ЭКСПЕРИМЕНТАЛЬНОЕ ИССЛЕДОВАНИЕ)

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РЕЗЮМЕ

Изучено состояние эндокринных клеток АПУД-системы в слизистой оболочке желудка. Исследование проведено с помощью световой и электронной микроскопии в экспериментальных условиях посредством стимуляции пентагастрином гематогенным путем. Установлена подчеркнутая гиперплазия и дегрануляция аргирофильных, и в особенности эндтерохромафиноподобных (ECL) клеток, коррелирующие с гиперплазией и высокой функциональной активностью пристеночных клеток железистой части желудка крыс. Гиперплазия и функциональная активность Д-клеток проявлены в более слабой степени. Встречаются единичные энтерохромафинные (ЕС) клетки.

В ответ на гастрин-стимулированной солянокислой секреции слизистая оболочка желудка выделяет слизь в избыточном количестве. Это является защитно-приспособительной реакцией стенки желудка, которая впоследствие ослабевает.

Полученные результаты раскрывают сложные взаимоотношения между эндокринными пристеночными клетками слизистой оболочки желудка. Они в значительной степени выявляют роль и значение секретируемых этими клетками гормонов в морфогенезе состояний сповышенной кислотностью, а также при язве двенадцатиперстной кишки.